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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/520,204

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EXAMINER

KUBELIK, ANNE R

ART UNIT

PAPER NUMBER

1638

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/520,204	Applicant(s) DANIELL, HENRY	
	Examiner Anne R. Kubelik	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 August 2008 and 06 October 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 11-14, 17 and 20-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 11-14, 17 and 20-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 13 August 2008 has been entered.
2. Claims 1-9, 11-14, 17 and 20-36 are pending.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
4. The objection to claim 31 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn in light of Applicant's amendment to the claim.

Claim Objections

5. Claim 9 remains objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. The objection is repeated for the reasons of record as set forth in the Office action mailed 13 March 2008X. Applicant's arguments filed 13 August 2008 have been fully considered but they are not persuasive.

Applicant urges that although the selection does not affect the structure of the genome, it affects which cellular organelle that genome is located (response pg 11-12).

This is not found persuasive because there is no limitation recited that affects the structure of the vector, because the plastid genome (and therefore any targeting sequences) is the same regardless of the type of plastid.

Claim Rejections - 35 USC § 112

6. Claim 13 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. Due to Applicant's amendment of the claims, the rejection is modified from the rejection set forth in the Office action mailed 13 March 2008. Applicant's arguments filed 13 August 2008 have been fully considered but they are not persuasive.

If in claim 13, Applicant is claiming the vector in a plant, the claim should be rewritten to claim a plant transformed by the vector. If, Applicant is not so claiming a plant, then the claim fails to further limit the parent claim.

Applicant urges that they have amended the claim (response pg 12-13).

This is not found persuasive for the reason indicated above. The location of the vector fails to further limit its structure.

Claim Rejections - 35 USC § 103

7. Claims 1-9, 11-14, 17 and 20-36 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Daniell et al (WO 01/64024) in view of Rathinasabapathi et al (1994, Planta 193:155-162). The rejection is repeated for the reasons of record as set forth in the Office action

Art Unit: 1638

mailed 13 March 2008. Applicant's arguments filed 13 August 2008 have been fully considered but they are not persuasive.

The claims are drawn to plastid transformation vectors encoding merA, merB and BADH.

Daniell et al teach a plastid transformation vector comprising a first flanking sequence (trnI), a promoter (16S Prn), a selectable marker (aadA), sequences encoding MerA and MerB arranged as an operon, a terminator (3' psbA), and a second flanking sequence (trnA) (Figs 8 and 12-13;), tobacco, Chlorella and Synechocystis thereby transformed, as well and progeny and seeds from the tobacco plants, and a method comprising exposing the plants to mercury (Figs 9-11; pg 30, line 2, to pg 35, line 9). The flanking sequences would be "conserved in the plastid genome of a plant species" and are from a transcriptionally active region. Daniell et al do not disclose BADH as the selectable marker.

Rathinasabapathi et al teach transformation of tobacco plants with a spinach or beet gene encoding BADH (pg 157). The protein is targeted to the chloroplasts (pg 157-158) and the resulting plants are resistant to betaine aldehyde (pg 159-160).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the plastid transformation vectors taught by Daniell et al, to use the BADH gene as a selectable marker as described in Rathinasabapathi et al. One of ordinary skill in the art would have been motivated to do so because of the suggestion of Rathinasabapathi et al to use betaine aldehyde resistance as a selectable marker in plants that lack glycine betaine (paragraph spanning the columns, pg 161) and because substitution of chloroplast transformation for chloroplast targeting of a nuclear-encoded gene is an obvious design choice.

Applicant urges that Rathinasabapathi et al teaches away from chloroplast transformation because although the plants metabolize betaine aldehyde at rates sufficient to confer resistance, their growth is still retarded (response pg 13-14).

This is not found persuasive. This does not teach away from chloroplast transformation. A teaching away from chloroplast transformation would be saying that expressing it from the plastid genome would not work. However, as the BADH protein is present and active in the chloroplast in Rathinasabapathi et al, there is no reason Rathinasabapathi et al or one of skill in the art would think that expression in the plastid would not work.

Applicant urges that Rathinasabapathi et al teaches that there was variation in BADH expression among constructs, meaning no expectation of success; one of skill in the art would expect even greater uncertainties if attempting chloroplast transformation (response pg 14).

This is not found persuasive. Variation in expression among constructs is normal. Two of the possible reasons Rathinasabapathi et al proposed for this variation, the polyA tail and the 3'UTR, would not be an issue in plastid transformation, as the polyA tail would not be present and a different 3' UTR would be used.

Applicant urges that the expression levels required to phytoremediate soils is higher than the levels required to confer resistance (response pg).

This is not found persuasive because Daniell et al teach phytoremediation of soils with plants whose plastids had been transformed with a plastid transformation vector comprising a first flanking sequence (trnI), a promoter (16S Prn), a selectable marker (aadA), sequences encoding MerA and MerB arranged as an operon, a terminator (3' psbA), and a second flanking

Art Unit: 1638

sequence (trnA) (see claim 33, for example). Applicant shows no unpredictability in use of BADH as a selection marker versus use of aadA.

Applicant urges that the specification states that no one to date has successfully transformed the plastid genome to ... bioremediate contaminant compounds, citing the inventor's recognition in the field (response pg 14-15).

This is not found persuasive because Daniell et al did so two years prior to the filing of the instant application (see claim 33, for example).

Applicant urges that Rathinasabapathi et al was published in 1994, and plastid transformation was made possible even earlier; Rathinasabapathi et al could have attempted to transform plastids and did not (response pg 15-16).

This is not found persuasive because not all labs have the gene gun apparatus, nor is the art required to reduce to practice every possible iteration of its teachings.

Applicant urges that during the time following Rathinasabapathi et al and following Daniell et al no one arrived at the claimed invention (response pg 16).

This is not found persuasive. Applicant appears to be arguing that a rejection under 103 is not possible because unless it was done in the prior art, an invention could not be obvious. This is not the case. Just because one of skill in the art did not actually make the claimed invention does not mean it was not obvious to do so.

Further, in response to applicant's argument based upon the age of the references, contentions that the references are old are not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977).

8. Claims 1-9, 11-14, 17 and 20-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniell (WO 99/10513) in view of Meagher et al (1999, US Patent 5,965,796), and further in view of Rathinasabapathi et al (1994, Planta 193:155-162). The rejection is repeated for the reasons of record as set forth in the Office action mailed 13 March 2008. Applicant's arguments filed 6 October 2008 have been fully considered but they are not persuasive.

The claims are drawn to plastid transformation vectors encoding merA and merB with BADH as the selectable marker.

Daniell disclose plastid transformation vectors comprising a first flanking sequence (trnI), a promoter (16S Prn or PatpB), a selectable marker (aadA or hyg-R), a sequence expressing a second protein (GFP or CryIIA), a terminator (3' psbA), and a second flanking sequence (trnA) (Fig 6-8). Hyg-R is an antibiotic-free selectable marker. trnI and trnA are sequences in a spacer regions and are highly conserved in plant species (pg 20, lines 20-25). Daniell et al disclose plants transformed with the vectors and progeny and seeds of those plants (pg 42, line 10, to pg 51, line 10; pg 57, line 1, to pg 60, line 36).

Daniell et al do not disclose merA and merB in those vectors or use of BADH as the selectable marker.

Meagher et al teach plants expressing both merA and merB (claims 2, 16, 18 and 26).

Rathinasabapathi et al teach transformation of tobacco plants with a spinach or beet gene encoding BADH (pg 157). The protein is targeted to the chloroplasts (pg 157-158) and the resulting plants are resistant to betaine aldehyde (pg 159-160).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the plastid transformation vectors taught by Daniell in view of Meagher et al, to use the BADH gene as a selectable marker as described in Rathinasabapathi et al and the express the merA and merB genes described in Meagher et al. One of ordinary skill in the art would have been motivated to do the latter because expression as an operon in the plastid would allow production of stoichiometric amounts of the two enzymes in the pathway. One of ordinary skill in the art would have been motivated to do the former because of the suggestion of Rathinasabapathi et al to use betaine aldehyde resistance as a selectable marker in plants that lack glycine betaine (paragraph spanning the columns, pg 161) and because substitution of chloroplast transformation for chloroplast targeting of a nuclear-encoded gene is an obvious design choice

Applicant urges that Meagher et al did not appreciate the advantage of expressing merA and merB as an operon would result in production of stoichiometric amounts; thus, one of even extraordinary skill in the art did not recognize this advantage (response pg 17-18).

This is not found persuasive. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Further, Meagher et al teach the advantages of expressing both proteins (column 12, lines 22-67); expression of both in the plastid would achieve this result.

Applicant urges that chloroplast transformation has been known since 1993, yet even those of even extraordinary skill in the art like Meagher et al and Rathinasabapathi et al failed to recognize the present invention (response pg 18).

This is not found persuasive. Applicant appears to be arguing that a rejection under 103 is not possible because unless it was done in the prior art, an invention could not be obvious. This is not the case. Just because one of skill in the art did not actually make the claimed invention does not mean it was not obvious to do so.

Applicant urges that those of ordinary skill in the art would have been discouraged by the combined teachings as well as failure of these predecessors to have achieved stable plastid transformation of a functional operon expressing two enzymes to phyto remediate mercury (response pg 18).

This is not found persuasive because Applicant has presented no evidence that any of Daniell, Meagher et al or Rathinasabapathi et al tried and failed to express merA and merB in plastids and failed. In contrast, Daniell shows a high expectation of success in expressing in plastids two open reading frames from the same promoter (pg 56-60). One of skill in the art would have no reason to think that merA and merB would act differently than the genes Daniell used, especially given that they are expressed as an operon in bacteria.

Conclusion

9. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114.

Art Unit: 1638

See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, Ph.D., whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

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November 5, 2008

/Anne R. Kubelik/

Primary Examiner, Art Unit 1638